REMARKS

The March 3, 2004 Official Action and references cited therein have been carefully reviewed. In light of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of the application are respectfully requested.

Claims 1-28 are pending in the application. Claims 3, 6-7, and 18-28 are cancelled in accordance with the Examiner's requirement.

The objection to the black boxes in Figure 24 has been maintained. Applicants submit herewith a publication quality Figure 24 which should serve to render the foregoing objection moot.

The Examiner has maintained the rejection of claims 15-17 under 35 U.S.C. §112 first paragraph, because plasmids pMSK45 and pMSK48 are allegedly not adequately described in the specification as filed.

Claims 1-2, and 8-14 remain rejected under 35 U.S.C. §112 first paragraph, as allegedly failing to meet the written description requirement. The Examiner has maintained her position that the downstream boxes of the claims are not adequately described. The Examiner urges that description of the structural features of a few exemplary downstream boxes does not adequately describe the genus of downstream boxes encompassed by the claims.

The Examiner has also maintained the rejection of claims 1-2, and 8-14 under 35 U.S.C. §112 first paragraph as allegedly lacking enablement. It is the Examiner's position that the downstream boxes recited in the claims encompass almost any sequence, and thus undue experimentation would be required to practice the invention.

The Examiner has maintained the rejection of claims 1-2,

4-5, and 8-14 under 35 U.S.C. §112 second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter of the invention.

Next, the Examiner has maintained the rejection of claims 1-2 under 35 U.S.C. §102(b). It is the Examiner's position that these claims are anticipated by Svab et al., (1993) PNAS 90:913-917 with evidence from Maliga et al, US Patent 5,877,402.

Further, the Examiner has maintained both rejections under 35 U.S.C. §102(e), as they pertain to claims 1-2, and 9. These claims are allegedly anticipated by Maliga et al, US Patent 5,877,402 with evidence from Jefferson (1993, Genbank Accession No. A00196). The claims are also allegedly anticipated by McBride et al., US Patent 6,271,444, with evidence from Barry et al., US Patent 5,627,061.

Finally, the Examiner notes that claims 4-5, 8, and 10-17 are free of the prior art. The Examiner also indicates that claims 4-5 would be allowable if amended to overcome the rejection under 25 U.S.C. §112 second paragraph, and to include all of the features of the base and intervening claims.

The foregoing constitutes the entirety of the objections and rejections raised in the March 3, 2004 Official Action. In light of the present claim amendments and the following remarks, each of the above-noted rejections under 35 U.S.C. §§ 112, first and second paragraph, and 102(b) and (e) is respectfully traversed.

CLAIMS 15-17 FULLY MEET THE ENABLEMENT REQUIREMENTS OF 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner rejected claims 15-17 as allegedly lacking enablement, because the plasmids must be obtainable by a

repeatable method set forth in the specification, or must be readily available to the public. If the plasmids are not so available or obtainable, a deposit is required.

The Examiner states that pMSK45 is a derivative of pMSK35 but that the specification fails to teach how it was made from pMSK35, or how it differs from pMSK35. The Examiner also states that while pMSK48 is made by inserting a fragment made using primers that encode a particular peptide, many different nucleic acids could encode the peptide, so the sequence is not taught.

Applicants again submit that plasmids pMSK45 and pMSK48 are sufficiently described in the specification as filed. As detailed in Applicants previous response, methods of making these plasmids are described at pages 79-85. At page 80, line 26 over to page 81, line 16, the components of plasmids pMSK45 and pMSK48 are characterized. First, contrary to the Examiner's assertion, the specification does describe how pMSK45 differs from the sequence of pMSK35 (which is provided in Figure 33 and encodes an aadA resistance marker flanked by rice plastid genome targeting sequences). pMSK45 is a derivative of pMSK35 which carries the PrrnLT7g10+DB/Ec promoter controlling a kanamycin resistance gene. The sequence for the promoter element is provided in SEQ ID NO: 14 and the kanamycin coding sequence is provided in US Patent 5,877,402 which has been incorporated into the specification. In light of the foregoing, it cannot be reasonably maintained that the skilled person having the instant specification before them would not be able to synthesize pMSK45 without undue experimentation. pMSK48 is generated by cloning *gfp* and *aadA* from plasmid pMSK41 into pMSK45 via an NheI-HindIII digestion. Inasmuch as the specification provides the full length sequences for the pMSK45 vector as well as the sequence

of the gfp/aadA fusion gene, it is respectfully submitted that plasmids pMSK45 and pMSK49 are fully described and enabled. Accordingly, a deposit is not required to practice the full scope of the invention and it requested that the rejection of claims 15-17 under 35 U.S.C. §112, first paragraph be withdrawn.

CLAIMS 1, 2, 5, AND 8-14 FULLY MEET THE WRITTEN DESCRIPTION REQUIREMENTS OF 35 U.S.C. § 112 FIRST PARAGRAPH

Claims 1, 2, and 8-14 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement. Applicants respectfully maintain, however, that the present specification includes written description more than sufficient to meet the statutory requirement.

The Examiner asserts that "almost any sequence is encompassed by the term "down stream box element". Applicants respectfully disagree.

Applicants urge that the down stream box elements as described in the present specification, must also possess the function of enhancing translation relative to a construct which lacks such a sequence element. These properties are recited in the claims. Therefore, the Examiner's assertion that almost any sequence will be encompassed by the present claim is unfounded as only sequences having sufficient homology will function as a downstream box and enhance translation of the operably linked coding sequence. Furthermore, extensive structural information which includes sequence information is provided is the specification. Additionally, methods for assessing the functionality of such downstream box elements is also provided. Again, at page 3, lines 3-11, exemplary bacterial downstream box elements are

described. Further, at pages 23-24, the specification teaches methods of determining a plastid downstream box element, including structural and functional information. Figures 1A and 2A-2B, depict exact sequence information for exemplary downstream box elements, and show the structure (size and complementarity) of these downstream box elements. Additionally, Figures 3A-3D show the sequences of numerous chimeric 5' regulatory regions which all comprise downstream box elements. Therefore the specification describes many specific downstream box element sequences, provides guidelines for determining other downstream box elements, such as complementarity to anti-downstream box regions, and provides a specific function associated with downstream box elements (i.e., enhanced translational efficiency.)

This combination of teachings meets the requirements for written description set forth in 35 U.S.C. §112, first paragraph, as a representative number of downstream box elements, as well as the general structure, and function of the downstream box is clearly disclosed, along with exemplary means of identifying a downstream box. Accordingly, Applicants submit that the claims are adequately described, and request withdrawal of the rejection.

CLAIMS 1, 2, AND 8-14 FULLY MEET THE ENABLEMENT REQUIREMENTS OF 35 U.S.C. § 112 FIRST PARAGRAPH

The Examiner has rejected claims 1, 2, and 8-14 as allegedly lacking enablement. Applicants respectfully traverse.

The Examiner again urges that a downstream box element encompasses a broad range of possible sequences, and therefore, it would require undue experimentation to determine

which downstream box elements would function as recited in the claims. However, as set forth above, the structure and function of a plastid downstream box is clearly described, and numerous specific examples of downstream boxes are disclosed in the specification. Therefore, from the teachings of the specification, it would require only routine experimentation to determine additional putative downstream box elements and test the same to determine their effect on translational efficiency.

Applicants again submit that use of conventional techniques in genetic engineering would allow a skilled artisan to develop constructs containing the putative downstream domains and then subsequently screen the constructs for enhanced translational efficiency. Exemplary techniques are outlined throughout the specification, particularly at pages 23-25, which describe downstream box element identification, construction, and screening. Further, Examples I-VIII all describe methods of constructing vectors comprising putative downstream box elements and determining translational efficiency as a function of reporter gene expression levels operably linked thereto.

The Examiner states that the specification must teach how to make the functional downstream elements, not how to find them. Applicants again submit that the specification does teach how to make these sequence elements. The structural information described extensively above, in combination with the methods for assessing functionality provided in the specification, provide the skilled artisan with all of the tools necessary to make (not just find) the downstream box elements encompassed by the present claims.

In light of the arguments presented herewith, Applicants respectfully submit that the invention is fully enabled and

request the withdrawal of the §112, first paragraph rejection of claims 1, 2, and 8-14.

CLAIMS 1, 2, 4, 5, AND 8-14 AS AMENDED FULLY MEET THE REQUIREMENTS OF 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 1, 2, 4, 5 and 8-14 as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicants respectfully traverse.

First, the Examiner maintains that it is unclear as to what the term "heterologous" is modifying in claim 1. As set forth in the previous response, Applicants respectfully submit that the term heterologous refers to the protein encoded by the coding region present in the recombinant DNA construct. By definition, as this protein is introduced into the plant on a recombinant DNA construct which is not native to the plant, such a protein would be considered heterologous, i.e., derived from a different source. Native proteins encoded by endogenous plant genes are not heterologous to a plant as they are not "derived" from a different source, i.e., a recombinant DNA construct. In other words, even if a tobacco protein were introduced into a tobacco plant, such a protein would still be heterologous to the tobacco plant as the protein encoded by the construct would be derived from a source not native to the plant. The fact that "heterologous" may refer to any number of proteins does not make the term vague and indefinite. Accordingly, Applicants request withdrawal of the rejection.

The Examiner also states that claim 1 lacks antecedent basis in the recitation of "said chimeric regulatory region". Applicants again submit that it is clear what the cited phrases refer to. However, in the interest of furthering prosecution, Applicants have amended the claim to provide

literal antecedent basis.

Next, the Examiner indicates claim 10 is indefinite for the recitation of "said fusion protein encoded by a first and second coding region". As exemplified in the specification, pMSK35 contains the coding region of the aadA gene operably linked to the gfp gene, both of which are driven by a single chimeric regulatory region. Indeed, claim 10 requires that production of the fusion protein is driven by the chimeric regulatory region. By definition, coding sequences which encode a "fusion protein" **are** operably linked and Applicants respectfully submit that there is nothing whatsoever unclear in claim 10 as currently drafted. Accordingly, it is submitted that the skilled person would be readily apprised of the subject matter encompassed by claim 10 and thus the rejection under 35 U.S.C. 112, second paragraph is inappropriate and should be withdrawn.

With regard to the Examiner's assertion that the sequences of the Markush group in claim 14 are very different, Applicants have removed the recitation of SEQ ID NO: 27 from the claim.

In view of the amendments presented herewith and the foregoing remarks, Applicants respectfully request the withdrawal of the rejection of claims 1, 2, 4, 5 and 8-14 under 35 U.S.C. §112, second paragraph.

CLAIMS 1, 2, AND 5 ARE NOVEL OVER SVAB ET AL., WITH EVIDENCE FROM US PATENT 5,877,402

The Examiner has maintained the rejection of claims 1, 2, and 5 under 35 U.S.C. §102(b) as allegedly anticipated by Svab et al.(PNAS (1993) 90:913-917) with evidence from US Patent 5,877,402. Applicants respectfully traverse.

MPEP §2131 sets forth the standard for a 102 rejection:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Examiner's interpretation of the language of claims 1, 2 and 9 flies in the face of the conventional understanding of molecular biology. The claims recite that regulatory region is **chimeric, contains the downstream box and is 5'** to the coding region of the heterologous protein. By definition and conventional understanding, such a sequence element cannot occur within the coding region after the occurrence of the ATG. Such a region would not be considered by the skilled person to **be 5' to the coding segment.** The specification teaches at page 5, lines 4-6 and lines 16-20 that expression of the coding region is driven by or regulated by the 5' chimeric regulatory region. Inasmuch as the Examiner acknowledges that the downstream box element of Svab et al. is within the coding region of the aadA gene, it cannot be reasonably maintained that this reference describes a construct which is identical to those presently claimed.

Inasmuch as Svab et al. fail to describe each and every element of the claimed invention, Applicants respectfully request the rejection of claim 1, and 2 under 35 U.S.C. §102(b) be withdrawn.

CLAIMS 1, 2, 5, AND 9 ARE NOVEL OVER US PATENT 5,877,402 WITH EVIDENCE FROM JEFFERSON

The Examiner has rejected claims 1, 2, and 9 under 35 U.S.C. §102(e) as allegedly anticipated by US Patent 5,877,402 (Maliga et al.) with evidence from Jefferson (1993, Genbank Accession No. A00196). Applicants respectfully traverse for the reasons set forth above in connection with the refutation

of the §102(b) rejection based on Svab et al. None of the constructs described in the foregoing references describe constructs comprising a **chimeric 5' regulatory region** comprising a leader sequence and downstream box element which is operably linked to a coding region for a heterologous protein. These references lack a downstream box element in the 5′ regulatory region.

In view of the foregoing remarks, Applicants respectfully submit that the '402 patent combined with Jefferson fails to anticipate the subject matter of the present invention. Accordingly, Applicants request the withdrawal of the rejection of claims 1, 2, and 9 under 35 U.S.C. §102(e).

CLAIMS 1, 2, 5, AND 9 ARE NOVEL OVER US PATENT 6,271,444 WITH EVIDENCE FROM US PATENT 5,627,061

The Examiner has rejected claims 1, 2, 5, and 9 under 35 U.S.C. §102(e) as allegedly anticipated by US Patent 6,271,444 (McBride et al.), with evidence from US Patent 5,627,061 (Barry et al.). Applicants respectfully traverse for the reasons set forth above.

Applicants submit that the teachings of the '444 patent do not meet all of the limitations of claims 1, 2, and 9 as amended. The constructs of the '444 patent do not comprise a chimeric 5' regulatory region comprising a downstream box element which is operably linked to and regulates the production of a heterologous protein.

Inasmuch as the '444 patent fails to describe each and every element of the claimed invention, Applicants respectfully request the rejection of claim 1, 2 and 9 under 35 U.S.C. §102(e) be withdrawn.

CONCLUSION

No new matter has been introduced into this application by reason of any of the amendments presented herewith. Moreover, none of the present claim amendments is believed to constitute a surrender of any originally claimed subject matter, or a narrowing of the claims in order to establish patentability. The effect of these amendments is merely to make explicit that which was implicit in the claims as originally worded.

It is respectfully requested that the amendments presented herewith be entered in this application, since the amendments are primarily formal, rather than substantive in nature. This amendment is believed to clearly place the pending claims in condition for allowance. In any event, the claims as presently amended are believed to eliminate certain issues and better define other issues which would be raised on appeal, should an appeal be necessary in this case.

It is respectfully urged that the rejections set forth in the March 3, 2004 Official Action be withdrawn and that this application be passed to issue. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

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Enclosures: New Figure 24 and Petition to Submit Color Photograph